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FUNCTIONAL STABILITY OF CEREBRAL CIRCULATORY SYSTEM

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16. Abstract: Functional stability of the cerebral circulation system seems to be based on the active mechanisms and on those stemming from specific of the biophysical structure of the system under study. This latter parameter has some relevant criteria for its quantitative estimation. The data obtained suggest that the essential part of the mechanism for active responses of cerebral vessels which maintains the functional stability of this portion of the bascular system, consists of a neurogenic component involving central nervous structures localized, for instance, in the medulla oblongata.			
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FUNCTIONAL STABILITY OF CEREBRAL CIRCULATORY SYSTEM

By Yu. Ye. Moskalenko*

The activity of the cardiovascular system as is known, experiences significant changes linked to the most diverse reasons governed by certain vital situations. This includes in the first place changes of an active nature that are caused by not always adequate reactions of the heart and vessels to physical and emotional loads. Another form of change, central hemodynamic shifts of a passive nature, occur during movements and changes in the body position in a vertical plane and mainly concern the systems of capacious vessels. Both types of changes in the indices of central hemodynamics are in explicit contradiction to the needs of a number of vitally important organs, in the first place the brain and kidneys that require an always intensive and little-changing influx of blood. /589**

The given contradiction developed, apparently, at certain stages of evolution, when the functional directivity of the central organs and circulatory systems that has consisted from the beginning of guaranteeing the circulation of the muscle and digestive system that changes in very broad limits, ceased

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to satisfy the need of the systems that developed in evolution later. Such systems primarily include the systems of controlling the activity of the organism and guaranteeing its water-saline homeostasis that has been studied the best--the central nervous system and the kidneys. An increase in their role /590 was one of the critical stages in the evolution of vertebrates.

A consequence of the contradiction of the functional directivity first developed in the process of evolution in the central region of the circulatory system and the needs of the organs and systems that developed at its subsequent stages, but on whose constant activity the condition of the organism as a whole depends, was the development of special mechanisms to stabilize the organ blood flow, its isolation from disturbances on the part of central hemodynamics. This includes mechanisms of both an active physiological nature that have been well studied in recent years in the examples of functioning of the vascular systems of the brain and kidneys during changes of perfusion pressure that have received the name "autoregulation of blood flow" [6, 14, 20], and of a passive nature that are governed by features of the biophysical structure of the vascular systems of these organs [8, 18]. The given mechanisms form an important property of the vascular basin in the examined group of organs; in their essence they are similar to the property of stability that is known for a broad class of complicated systems [1, 2], the capacity to withstand external disturbances or functional stability of the system of organ circulation. This concept consequently characterizes the capacity of the organ vascular mechanisms to fulfill their functional task, namely, maintenance of organ homeostasis or circulatory support of the organs on the background of a change in the activity of the central divisions of the cardiovascular system with regard for the changing metabolic needs of individual sections of the organ, and even possibly, individual

cellular assemblies. This property of certain regional vascular basins is important in the most diverse external effects and conditions of the organism that are often reduced to a change in organ perfusion pressure and chemistry of the blood. Here the task consists not only of maintaining the necessary minimum supply of nutrients, but also preserving the organ from surplus blood supply, since the latter is important in terms of saving the general consumption of blood and as a measure of preserving organ vessels from excessive pressure differentials. It follows from here that an assessment of the functional stability of a certain regional vascular basin, as well as observation of its dynamics can be an objective criterion for the effective fulfillment by them of their functional task during certain effects on the organism or its different conditions. The common nature of this concept on stability for the most diverse types of complicated systems opens up additional possibilities for approaches to solving certain problems of physiology of regional circulation, by using the currently well-developed methods and approaches of research on complicated systems, taking into consideration naturally, the specific nature of the structural-functional organization of each specific regional vascular basin.

In relation to what has been said this article has the goal of viewing the applicability of the aforementioned general concepts on the functional stability of organ circulation in the example of one of the particular problems, namely, the features of circulatory support for the activity of the brain as a single functional link under altered conditions of influx or efflux of blood from the cranium, after focusing especial attention on the role of the central regulatory mechanism in this process.

TECHNIQUE

A study of the functional stability of organ vascular mechanisms with the use of principles, methods and approaches of investigating complicated systems, including mathematical modeling (which has already justified itself in solving a number of questions of the physiology of cerebral circulation [7]), first of all requires the detection of means by which the disturbing factors that affect the examined functional unit enter on the part of other systems of the organism or "inlets" of the studied system and communication canals of the result of its functioning with other functional units, or its "outlet." As applied to the system of intracranial circulation its "inlets" are the levels of system arterial and venous pressure, and the "outlet" is the average intensity of the cerebral blood flow. An evaluation of the functional stability is reduced to a certain method of studying the systems, namely, clarification of the features of amplitude and time relationships between the changes in the levels of "inlets" and "outlet" of the system during a dosed effect on its "inlets." The latter, evidently, can be attained with the help of directed functional loads. /591

Thus, a study of the characteristics of the functional stability of the cerebral circulatory system is reduced to a simultaneous recording of two groups of indices--systems arterial and venous pressure on the one hand, and average intensity of cerebral blood flow on the other. If the recording of the first of the indicated groups of indices can be accurately and dynamically implemented to a sufficient degree with the help of electromanometers of different designs, then the most adequate for recording the average intensity of cerebral blood flow is the combination of one of the known modifications of the Klirens technique, quantitative, but discrete, with qualitative, but dynamic technique, for

example with electroplethysmography, that mutually supplement each other [4, 17].

As functional tests to evaluate the limit and completeness of functional stability in the cerebral circulatory system one can use orthostatic effects, the tests of Val'sal'va, Kvekkenshtedt, short-term pinching of the carotid artery and other effects that alter the conditions of influx and efflux of blood from the cranium, or the characteristics of central hemodynamic activity. In analyzing the obtained results one should take into consideration several indices that afford the possibility of approaching a quantitative evaluation of the condition of functional stability of the cerebral circulatory system according to the features of the relationship for it of "pressure-blood flow" in the generalized form indicated in Figure 1. Such indices primarily include the limits of functional stability 1, lower and upper boundaries for the effectiveness of regulatory mechanisms 2 and 3, angle of incline of the plateau of curve 4. If the first three indices characterize the limits of the functional stability, the fourth indicates its quality. In evaluating the features of the dynamics for functional stability of the cerebral circulatory system in certain experimental conditions, or with different conditions of the organism it is convenient to use a special coefficient that is derived on the basis of the autoregulation index [11],
$$K = 1 - \frac{R_0 \cdot \Delta P - P_0 \cdot \Delta R}{\Delta P (R_0 + \Delta R)},$$
 where K--coefficient that characterizes the functional stability of the studied system, R_0 and P_0 --initial values of resistance and pressure in the cerebral vessels, ΔR and ΔP --changes in these amounts with certain effects on the studied system. With $K=0$ --there is no functional stability; $K>0$ indicates the presence of regulatory processes directed towards maintaining functional stability of the examined system, where with $K \leq 1$ the functional stability is reduced, while

$K > 1$ designates hypercompensation. Complete functional stability is characterized by the value $K=1$, while $K < 0$ characterizes distorted reactivity.

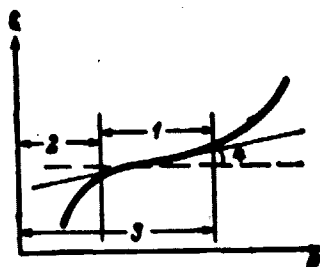


Figure 1. Generalized Curve Characterizing the Functional Stability of the Cerebral Circulatory System and Certain Criteria for Evaluating It.

Key:

- | | |
|--|---------------|
| 1. limits of functional stability | P. pressure |
| 2,3. its lower and upper limits respectively | Q. blood flow |
| 4. index for quality of functional stability | |

A study of the physiological mechanisms that are at the basis of the functional stability of the cerebral circulatory system in the first place requires observation of the features of its dynamics with the help of the techniques listed above, according to the indices presented in Figure 1, with directed effects on certain elements of the studied system with the help of procedures that have long been entrenched in the practice of physiological research--mechanical or chemical damage to individual structural links in order to disengage them from participating in the studied processes, as well as physical or chemical stimulation of individual structural elements in the system in order to detect their functional importance.

All that has been stated mainly concerns the method aspects of the general plan, that are sometimes no less important than analysis of particular techniques. The cited discussion on the principle of the approach are applicable evidently,

not only for an investigation of the vascular basin of the brain, and indicate that a systems approach introduces a significant organizing principle already at the stage of setting up the study, making it possible to reduce the known techniques and experimental approaches to a precise plan.

RESULTS OF STUDY AND THEIR DISCUSSION

Extensive factual material that has been accumulated by now on the functioning of the vascular cerebral mechanisms, including our data that were obtained recently, is distinguished by very different plans and nonuniform coverage of individual questions. However its analysis with regard for the principles of the systems approach to the study make it possible to isolate several groups of facts that indicate both the features of the functional stability of the cerebral circulatory system, and the physiological mechanisms that are at its basis.

1. Under normal physiological conditions the total cerebral blood flow remains practically constant during changes in the systems arterial pressure in limits from 60-180 mmHg; with changes in the intracranial or venous pressures in limits of 15-80 mmHg, or changes in both of the indices such that the perfusion pressure through the brain could not fall below 40 mmHg [6, 22, 9]. A study of the temporal indices for the mechanisms that are at the basis of the functional stability of the cerebral circulatory system demonstrated that the time for its triggering is a fairly constant amount in each specific experiment, fluctuating in different animals from 25 to 60 s [6]; in man under normal physiological conditions it is 15-30 s. The studies conducted from a comparative physiological aspect demonstrated that active physiological reactions directed towards normalization of blood filling of the cranial cavity (Figure 3) are observed for the first time at the level of higher reptiles [10]. /593

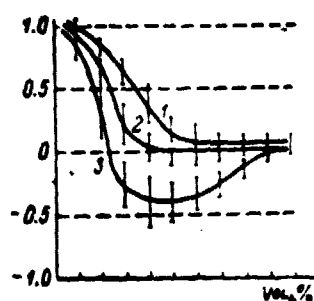


Figure 2. Dynamics for the Coefficient that Characterizes the Functional Stability of the Cerebral Circulatory System with Different Types of Narcosis

Key:

1. ether
2. barbiturates
3. fluorothan

on x axis--concentration of narcosis in con. un.

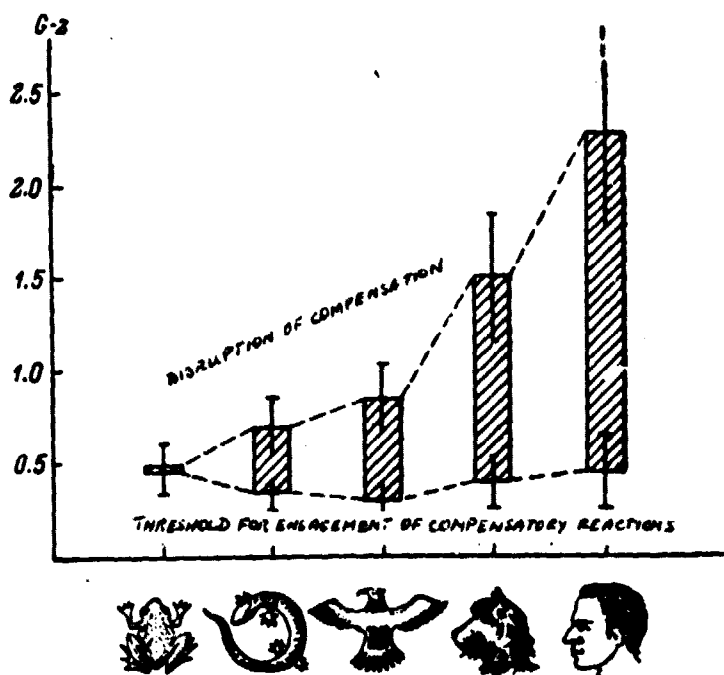


Figure 3. Limits of Functional Stability of Cerebral Circulatory System in Representatives of Certain Species of Vertebrates with Longitudinal Gravity Load (GZ in leg-head direction)

2. The coefficient that characterizes the functional stability under normal physiological conditions close to a unit significantly changes in different situations, which indicates the dynamics of the functional stability in the examined system. Thus, it undergoes complicated changes during different types of narcosis (Figure 2), gradually passing from the phase of complete functional

stability to the phase of its decline, and further--disappearance of the active regulatory component. The given fact indicates in turn the importance of selecting experimental conditions to study the phenomenology of functional stability in the cerebral circulatory system.

3. The lower and upper limits of functional stability, as well as the incline of the curve plateau undergo significant changes when different links of the central regulatory mechanisms are affected. Thus, during desympathization the lower limit is changed in the functional stability, at the same time the primary effect observed immediately after disengagement of the sympathetic innervation significantly differs from the effect observed in later periods [15, 21]. The condition of functional stability can be altered during a number of external effects, which is indicated in particular by facts on the dynamics of intracranial human rheograms (Figure 4) in response to functional loads recorded in different periods of a space flight [19]. The functional stability is significantly altered in a number of pathological conditions, for example, during cranial-cerebral injury [14, 20]; here observation of its characteristics, in our opinion, can provide valuable information in terms of optimizing the therapeutic measures.

4. The features of biophysical structure of the cerebral circulatory system that consist of a constant amount of fluid in the closed cranial cavity and the possibility of efflux of a certain volume of liquor from the cranial cavity into the vertebral cavity through an opening of restricted diameter [8] determine in certain limits the low critical level of the relationship between the total hydrodynamic resistance of the cerebral vascular system and arterial pressure. This property that was shown for the first time by calculations on simple models

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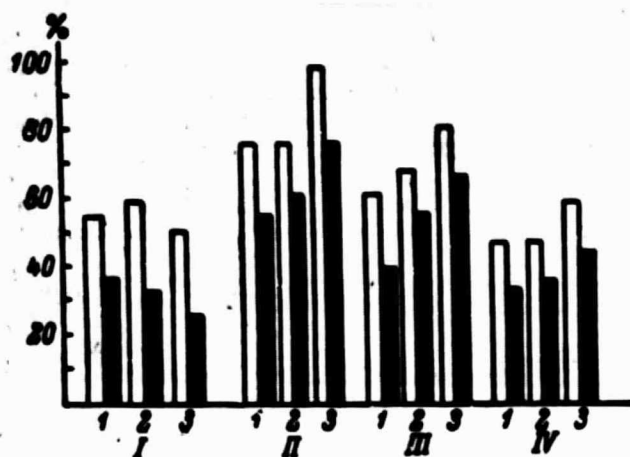


Figure 4. Dynamics for Functional Stability of Cerebral Circulatory System in Different Periods of Spaceflight (according to data from processing intracranial rheograms recorded in crew member of orbital station "Salyut-4" V. I. Sevast'yanov).

Key:

- I. before flight
- II. eighth day of flight
- III. twentieth day of flight
- IV. fifth day after flight

white column--before load

black columns--after load

- 1, 2, 3. indices of rheoencephalograms indirectly characterizing condition of large arteries, small arteries and veins of the brain respectively. As a functional load negative pressure was used applied to the lower half of the body.

and confirmed by further studies [8, 10], in turn provides the basis for a conclusion that the functional stability of the cerebral circulatory system has at its basis also a passive biochemical mechanism. Although it is still difficult to provide a conclusion about the boundaries for the effectiveness of the given mechanism, the results of modeling the intracranial biomechanics [8] provide the grounds to hypothesize that the biomechanical phenomena promote the maintenance of functional stability in the cerebral circulatory system with low levels of arterial pressure, and apparently determine its loss with a further reduction in arterial pressure.

The cited four groups of facts demonstrate thus, that the concept we proposed that by analogy with a similar property in complex systems was called the functional stability of the cerebral circulatory system, characterizes the property of the cerebral vascular system that has been acquired through evolution and consists of the capacity to guarantee natural circulatory homeostasis. In its meaning and physiological importance this concept has been accepted more broadly in recent years than the concept of "autoregulation of blood flow," since it refers not only to perfusion pressure, but also to other indices, for example blood chemistry. It is also distinguished by the fact that a rich method arsenal of studying a similar property in the most diverse complicated systems is applicable for its study and evaluation. Although the use of such an approach to studying the functional stability of the cerebral circulatory system is in the beginning phase, and a lot of work remains to clarify the boundaries of applicability of certain methods of stability evaluation to solving physiological tasks, even now one can conclude that this is a constructive method for generating objective criteria to evaluate the given property of physiological systems. Thus, based on the facts given above one can conclude that the indices presented in Figure 1 reflect the quantitative aspect of the adaptation capacities of the studied system, while the temporary characteristics indicate the rate of transition from one condition to another during different effects on the organism, and the rate of normalization after the effect has stopped or the lability of the regulatory processes. Although the factual material that has been accumulated by now does not yet make it possible to reveal all the features of the information content of each of the examined indices (this requires further directive study), one can expect already on the basis of the data given above that ideas on the functional stability will be useful for investigating the effect on the

organism of different external factors, as well as to optimize therapeutic procedures on a number of pathological conditions.

In touching upon the question of the mechanisms at the basis of functional stability of the cerebral circulatory system, one should note that the known materials indicating the nature of their active component are very vast [5, 8, 20] and they can be presented in the form of the following groups of facts: a) data on the presence of adrenergic and cholinergic effects on cerebral vessels representing the results of morphological studies that indicated the presence of rich innervation in the walls of the cerebral vessels of all levels, all the way to precapillaries, as well as experiments that reveal the sensitivity of the cerebral vessels to specific mediators and detected the presence of direct responses of the cerebral vessels during electrical stimulation or cutting of the sympathetic and parasympathetic nerve fibers; b) morphological data on the presence of a broad representation in different segments of the cerebral vascular system, in the dura mater, in the main arteries that deliver blood to the brain /595 of the receptor zones, as the minimum of two modalities--baro-and chemo-receptors; c) data of a physiological plan on the sensitivity of cerebral vessels to different chemical factors formed in the process of cerebral activity, as well as materials that indicate the direct sensitivity of cerebral vascular walls to a change in intracerebral pressure.

These data make it possible to isolate a number of regulatory effects on cerebral vessels, that, by using principles of systems approach, can be presented in the form of a plan shown in Figure 5. This plan clearly reveals several contours of regulation that are characterized both by direct paths of influence on the vessels, and by chains of feedback that correspond to myogenic,

metabolic and neurogenic mechanisms for regulating cerebral circulation. These mechanisms recently were extensively discussed in the literature and at times contrasted with each other. The given plan shows that the latter is hardly correct, since the regulatory structure that it formalizes, that includes several contours of regulation, should possess significantly greater reliability in terms of guaranteeing functional stability of the examined system, than if it was based on any one regulatory contour. It is logical to conclude that the greatest regulatory potentialities in the plan shown in Figure 5 are found in the neurogenic mechanism, in which the adrenergic and cholinergic innervation should be viewed as paths for transmitting the regulatory effect to the executive link, the smooth muscle of the vessel, while the receptor zones mentioned above are the receiving links in the neurogenic contour of regulation that apparently /596 include the central nervous formation. The latter is indicated, for example, by the data given above on the easy susceptibility to damage of the mechanisms for functional stability of the cerebral circulatory system during narcosis, the effect on it of specific afferent impulses developing under conditions of space flight. A large number of researchers share the opinion on the participation of central nervous formations in regulating cerebral circulation; at the same time there are still direct indications of the localization of these formations [13, 16]. More problematic is the question of the link between the central neurogenic component for the mechanism of functional stability of the cerebral circulatory system, and the mechanism for regulation of the system's arterial pressure. However indications have recently appeared not only of their difference, but even the reciprocity of interrelationships between the central regulations of the system's arterial pressure and cerebral circulation [3]. Thus, one can draw a conclusion with a high degree of probability that the central

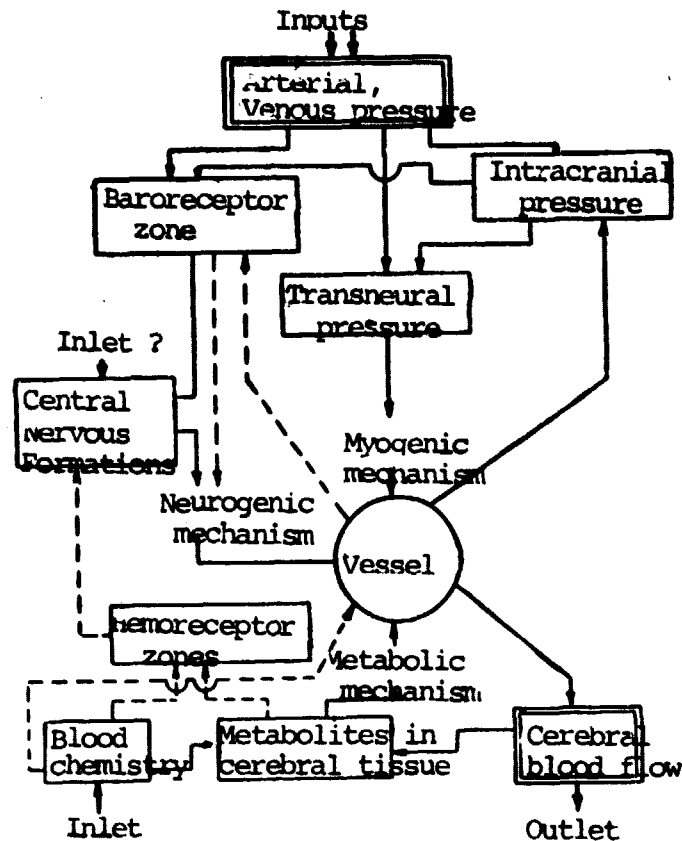


Figure 5. Functional Plan for Regulatory Effects on Cerebral Vessels Constructed from Positions of Systems Approach

Dotted lines show the links whose existence is still hypothetical.

neurogenic link is one of the main mechanisms at the basis of functional stability of the cerebral circulatory system, but the question of the nerve formations realizing it and their interrelationship with the vasomotor center of the medulla oblongata still remains very problematic.

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